PATENT

Docket No.: ISIS-1158

Please amend claims 1, 5, 8-10, 12, 13, 15, 20, 23, 24, 30, 47-49, 51, and 52 as follows:

(amended three times) A peptide nucleic acid conjugate comprising:

a backbone formed of amino alkyl amino acid monomeric units linked through amide bonds;

said backbone having an amino end, a carboxyl end, a plurality of said amino alkyl amino acid monomeric units, and a conjugate bound directly or through a linking moiety to at least one of said amino end or said carboxyl end;

each of said amino alkyl amino acid monomeric units having a tethered nucleobase:

said conjugate being a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, or a porphyrin.

5. (twice amended) A peptide nucleic acid conjugate comprising:

a backbone formed of amino alkyl amino acid monomeric units linked through amide bonds:

said backbone having an amino end, a carboxyl end, a plurality of said amino alkyl amino acid monomeric units,

each of said amino alkyl amino acid monomeric units having a tethered nucleobase: and

a conjugate bound to one of said nucleobases or its said tether either directly or through a linking moiety, wherein said conjugate is a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers.

8. (amended twice) A peptide nucleic acid conjugate of claim 53 wherein said conjugate includes a linking moiety.

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- (amended twice) A peptide nucleic acid conjugate of claim 53 wherein at least one group R¹² is a conjugate.
- 10. (amended three times) A peptide nucleic acid conjugate of claim 53 wherein at least one of L and L_m is $R^{12}(R^{13})_1$ is a conjugate.
- 12. (amended twice) A peptide nucleic acid conjugate of claim 54 wherein at least one of said A-A_m groups include at least one of R¹, R², and R³.
- 13. (amended twice) A peptide nucleic acid conjugate of claim 54 wherein at least one of $B-B_m$ groups or said $G-G_m$ groups include at least one group \mathbb{R}^3 .
- (amended twice) A peptide nucleic acid conjugate of claim 53 wherein at least one of said groups Q or I include at least one of groups R⁸, R⁹, R¹⁰, and R¹¹.
- 20. (amended twice) A peptide nucleic acid conjugate of claim 53 wherein m is from 1 to about 20.
- (amended twice) A peptide nucleic acid conjugate of claim 62 wherein R¹² is a conjugate.
- 24. (amended three times) A peptide nucleic acid conjugate of claim 62 wherein a is 1.
- 30. (amended four times) A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:

or the formula

or the formula

wherein:

L is R¹²(R¹³)_a; wherein:

 R^{12} is hydrogen, hydroxy, (C_1 - C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group;

R¹³, if present, is a conjugate;

provided at least one R12 and R13 is a conjugate; and

a is 0 or 1;

K is (CR⁶R⁷)₂;

J is (CR⁶R⁷), wherein:

 R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2\text{-}C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1\text{-}C_6)$ alkoxy, $(C_1\text{-}C_6)$ alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio or amino;

 R^5 is hydrogen, a conjugate, $(C_1\text{-}C_6)$ alkyl, hydroxy-, alkoxy-, or alkylthio- substituted $(C_1\text{-}C_6)$ alkyl:

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

Lis an integer from 1 to 5; and

at least one of L and R³ comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers:

wherein said conjugate optionally includes a linking moiety.

47. (twice amended) A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:

or the formula

or the formula

wherein:

L is R¹²(R¹³)_a; wherein:

 R^{12} is hydrogen, hydroxy, (C₁-C₄)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group;

R13, if present, is a conjugate; and

a is 0 or 1;

K is $(CR^6R^7)_{r}$:

J is (CR6R7)y; wherein:

 R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2$ - $C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1$ - $C_6)$ alkoxy, $(C_1$ - $C_6)$ alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

 R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino;

 R^5 is hydrogen, a conjugate, $(C_1\text{-}C_6)$ alkyl, hydroxy-, alkoxy-, or alkylthiosubstituted $(C_1\text{-}C_6)$ alkyl;

. each of y and z is zero or an integer from 1 to 10, the sum y+z being greater than 2 but not more than 10:

l is an integer from 1 to 5; and

at least one of L and R³ comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and wherein at least one of R³, R⁴, R⁵, R⁶, and R⁷ is a conjugate.

48. (twice amended) A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:

or the formula

or the formula

wherein:

L is R12(R13)a; wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group.

R13, if present, is a conjugate; and

a is 0 or 1;

K is (CR6R7)2;

J is (CR6R7), wherein:

 R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2\text{-}C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy. $(C_1\text{-}C_6)$ alkoxy, $(C_1\text{-}C_6)$ alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

 R^3 and R^4 independently are hydrogen, a conjugate, $(C_1$ - $C_4)$ alkyl, hydroxy- or alkylthio-substituted $(C_1$ - $C_4)$ alkyl, hydroxy, alkoxy, alkylthio or amino;

 $R^{5} \ is \ hydrogen, \ a \ conjugate, \ (C_{1}-C_{6}) \\ alkyl, \ hydroxy-, \ alkoxy-, \ or \ alkylthiosubstituted \ (C_{1}-C_{6}) \\ alkyl;$

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

l is an integer from 1 to 5; and

at least one of L and R³ comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein at least one of said group K or said group J includes a conjugate.

49. (twice amended) A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:

or the formula

or the formula

wherein:

L is R12(R13)a; wherein:

 R^{12} is hydrogen, hydroxy, (C_1 - C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group.

PATENT

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R13, if present, is a conjugate; and

a is 0 or 1;

K is $(CR^6R^7)_{r}$:

J is (CR6R7), wherein:

 R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid. (C_2 - C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1 - C_6) alkoxy. (C_1 - C_6) alkylthio, a conjugate, NR^5R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

 R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy- alkylthio or amino;

 $R^5 \ is \ hydrogen, \ a \ conjugate, \ (C_1-C_6) alkyl, \ hydroxy-, \ alkoxy-, \ or \ alkylthiosubstituted \ (C_1-C_6) alkyl;$

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10:

l is an integer from 1 to 5; and

at least one of L and R³ comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers.

wherein said conjugate optionally includes a linking moiety: and wherein said group R^3 is a conjugate.

- 51. (amended) A peptide nucleic acid conjugate of claim 53 wherein one of Q or I comprises a conjugate, wherein said conjugate is polylysine.
- 52. (amended) A peptide nucleic acid conjugate of claim 53 wherein one of A, A_m , L or L_m comprises a conjugate, wherein said conjugate is polylysine.

Please add new claims 53, 54, 55, 56, 57, 58, 59, 60, 61, and 62.

53. (new) A peptide nucleic acid conjugate of the formula:

wherein:

m is an integer from 1 to about 50;

L and L_m independently are $R^{12}(R^{13})_a$ wherein:

 R^{12} is hydrogen, hydroxy, (C_1-C_4) alkanoyl, a naturally occurring nucleobase, a nonnaturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobasebinding group, a heterocyclic moiety, a reporter ligand, or a conjugate:

provided that at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group.

R¹³, if present, is a conjugate;

provided at least one R12 and R13 is a conjugate; and

a is 0 or 1;

C and C_m independently are (CR⁶R⁷)_y; wherein:

 R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2 \cdot C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1 \cdot C_6)$ alkoxy, $(C_1 \cdot C_6)$ alkylthio, a conjugate, NR^3R^4 , SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

wherein R^5 is hydrogen, a conjugate, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthiosubstituted (C_1-C_6) alkyl; and

 R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino;

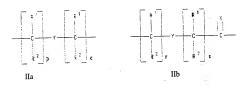
D and D_m independently are (CR⁶R⁷)_z;

each of y and z is zero or an integer from 1 to 10, wherein the sum y + z is greater than 2 but not more than 10:

 $G_m \ is \ independently \ -NR^3CO-, \ -NR^3CS-, \ -NR^3SO-, \ or \ -NR^3SO_2- \ in \ either \ orientation;$

each pair of $A\text{-}A_m$ and $B\text{-}B_m$ are selected such that:

- (a) A or A_m is a group of formula (Πa), (IIb) or (IIc) and B or B_m is N or R³N+; or
- (b) A or A_m is a group of formula (IId) and B or B_m is CH:



where:

X is O, S, Se, NR3, CH2 or C(CH3)2;

Y is a single bond, O, S or NR4;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

 $R^1 \ and \ R^2 \ independently \ are \ hydrogen, (C_1-C_4) alkyl, \ hydroxy-substituted (C_1-C_4) alkyl, \ alkoxy-substituted (C_1-C_4) alkyl, \ alkylthio-substituted (C_1-C_4) alkyl, \ hydroxy, \ alkoxy, \ alkylthio, \ amino, \ halogen \ or \ a conjugate;$

IId

I is $-NR^8R^9$ or $-NR^{10}C(O)R^{11}$; wherein:

 R^3, R^9, R^{10} and R^{11} independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate;

 $Q~is~-CO_2H.~-CO_2R^8,~-CO_2R^9,~-CONR^8R^9,~-SO_3H,~-SO_2NR^{10}R^{11}~or~an~activated derivative~of~-CO_2H~or~-SO_3H;~and$

wherein:

at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A, A_m , L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers:

wherein said conjugate optionally includes a linking moiety.

54. (new) A peptide nucleic acid conjugate of the formula:

wherein:

m is an integer from 1 to about 50;

L and L_m independently are R¹²(R¹³)_a wherein:

R¹² is hydrogen, hydroxy, (C₁-C₄)alkanoyl, a naturally occurring nucleobase, a nonnaturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobasebinding group, a heterocyclic moiety, a reporter ligand, or a conjugate:

provided that at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group;

R13, if present, is a conjugate; and

a is 0 or 1:

C and C_m independently are $(CR^6R^7)_y$; wherein:

 R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2 \cdot C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1 \cdot C_6)$ alkoxy, $(C_1 \cdot C_6)$ alkylthio, a conjugate, NR^3R^4 , SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

wherein R^5 is hydrogen, a conjugate, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthiosubstituted (C_1-C_6) alkyl; and

 R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino:

D and D_m independently are (CR⁶R⁷)_z;

each of y and z is zero or an integer from 1 to 10, wherein the sum y + z is greater than 2 but not more than 10;

 G_m is independently -NR 3 CO-, -NR 3 CS-, -NR 3 SO-, or -NR 3 SO-: in either orientation:

each pair of A-A_m and B-B_m are selected such that:

- (a) A or A_m is a group of formula (IIa), (IIb) or (IIc) and B or B_m is N or R^3N^* ; or
- (b) A or Am is a group of formula (IId) and B or Bm is CH;

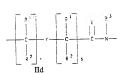




IIa

IIb





wherein:

X is O. S. Se, NR3, CH2 or C(CH3)2;

Y is a single bond, O, S or NR4:

each of p and q is zero or an integer from 1 to 5:

each of r and s is zero or an integer from 1 to 5;

 R^1 and R^2 independently are hydrogen, (C_1-C_4) alkyl. hydroxy-substituted (C_1-C_4) alkyl. alkoxy-substituted (C_1-C_4) alkyl, alkylthio-substituted (C_1-C_4) alkyl, hydroxy. alkoxy, alkylthio, amino. halogen or a conjugate;

I is -NR⁸R⁹ or -NR¹⁰C(O)R¹¹; wherein:

R⁸, R⁹, R¹⁰ and R¹¹ independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleotide, a soluble polymer, a non-soluble polymer or a conjugate;

 Q_{1S} -CO $_2$ H, -CO $_2$ R 8 , -CO $_2$ R 9 , -CONR 8 R 9 , -SO $_3$ H, -SO $_2$ NR 10 R 11 or an activated derivative of -CO $_2$ H or -SO $_3$ H: and

wherein:

at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator, or

at least one of A, A_m , L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers:

wherein said conjugate optionally includes a linking moiety; and wherein at least one of \mathbb{R}^1 , \mathbb{R}^2 or \mathbb{R}^3 is a conjugate.

(new) A peptide nucleic acid conjugate of the formula:

wherein:

55.

m is an integer from 1 to about 50;

L and L_m independently are $R^{12}(R^{13})_a$ wherein:

 R^{12} is hydrogen, hydroxy, (C_1-C_4) alkanoyl, a naturally occurring nucleobase, a nonnaturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobasebinding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

provided that at least one of R¹² is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group:

R13, if present, is a conjugate; and

a is 0 or 1;

C and C_m independently are $(CR^6R^7)_y$; wherein:

 R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2 \cdot C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1 \cdot C_6)$ alkoxy, $(C_1 \cdot C_6)$ alkylthio, a conjugate, NR^3R^4 , SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system:

wherein \mathbb{R}^5 is hydrogen, a conjugate, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthiosubstituted (C_1-C_6) alkyl; and

 R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino;

D and D_m independently are (CR⁶R⁷)_z;

each of y and z is zero or an integer from 1 to 10, wherein the sum y + z is greater than 2 but not more than 10;

G_m is independently -NR³CO-, -NR³CS-, -NR³SO-, or

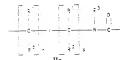
-NR3SO - in either orientation;

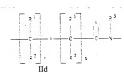
each pair of A-Am and B-Bm are selected such that:

- (a) A or A_m is a group of formula (IIa). (IIb) or (IIc) and B or B_m is N or R^3N^* ; or
- (b) A or A_m is a group of formula (IId) and B or B_m is CH;









wherein:

X is O, S. Se, NR3, CH2 or C(CH3)2:

Y is a single bond, O, S or NR⁴;

each of p and q is zero or an integer from 1 to 5:

each of r and s is zero or an integer from 1 to 5;

 R^1 and R^2 independently are hydrogen, (C_1-C_4) alkyl, hydroxy-substituted (C_1-C_4) alkyl, alkoxy-substituted (C_1-C_4) alkyl, alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate:

I is -NR8R9 or -NR10C(O)R11; wherein:

R⁸, R⁹, R¹⁰ and R¹¹ independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate;

 Q_{1S} -CO $_2$ H, -CO $_2$ R 8 , -CO $_2$ R 9 , -CONR 8 R 9 , -SO $_3$ H, -SO $_2$ NR 10 R 11 or an activated derivative of -CO $_2$ H or -SO $_3$ H; and

wherein:

at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator: or

at least one of A, A_m , L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers:

wherein said conjugate optionally includes a linking moiety; and wherein at least one of \mathbb{R}^8 , \mathbb{R}^9 , \mathbb{R}^{10} and \mathbb{R}^{11} is a conjugate.

56. (new) A peptide nucleic acid conjugate of the formula:

wherein:

m is an integer from 1 to about 50;

L and L_m independently are $R^{12}(R^{13})_a$ wherein:

 R^{12} is hydrogen, hydroxy, (C_1-C_4) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

provided that at least one of \mathbb{R}^{12} is a naturally occurring nucleobase, a nonnaturally occurring nucleobase, or a nucleobase-binding group;

R13, if present, is a conjugate; and

a is 0 or 1:

C and C_m independently are (CR⁶R⁷)_y; wherein:

 R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2 \cdot C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1 \cdot C_6)$ alkoxy, $(C_1 \cdot C_6)$ alkoxy, $(C_1 \cdot C_6)$ alkylthio, a conjugate, NR^3R^4 . SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system:

wherein R^5 is hydrogen, a conjugate, $(C_1\text{-}C_6)$ alkyl, hydroxy-, alkoxy-, or alkylthio- substituted $(C_1\text{-}C_6)$ alkyl; and

 R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino;

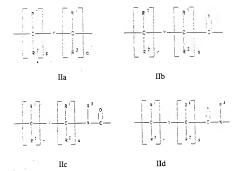
D and D_m independently are (CR⁶R⁷)_z;

each of y and z is zero or an integer from 1 to 10, wherein the sum y + z is greater than 2 but not more than 10;

 G_m is independently -NR 3 CO-, -NR 3 CS-, -NR 3 SO-, or -NR 3 SO₂- in either orientation:

each pair of A-A_m and B-B_m are selected such that:

- (a) A or A_m is a group of formula (IIa), (IIb) or (IIc) and B or B_m is N or R^3N^{τ} ; or
- (b) A or A_m is a group of formula (IId) and B or B_m is CH:



wherein:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂; Y is a single bond, O, S or NR⁴; each of p and q is zero or an integer from 1 to 5:

each of r and s is zero or an integer from 1 to 5;

 R^1 and R^2 independently are hydrogen, (C_1-C_4) alkyl, hydroxy-substituted (C_1-C_4) alkyl, alkoxy-substituted (C_1-C_4) alkyl, alkylthio-substituted (C_1-C_4) alkyl, hydroxy. alkoxy, alkylthio, amino, halogen or a conjugate:

Lis -NR 8R9 or -NR 10C(O)R11: wherein:

R⁸, R⁹, R¹⁰ and R¹¹ independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate:

Q is -CO₂H, -CO₂R⁸, -CO₂R⁹, -CONR⁸R⁹, -SO₃H, -SO₂NR¹⁰R¹¹ or an activated derivative of -CO₂H or -SO₄H; and

wherein:

at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A, A_m , L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety: and wherein at least one of R³ R⁴, R⁵, R⁶ and R⁷ is a conjugate.

 (new) A peptide nucleic acid conjugate comprising a plurality of monomers of formula:

wherein:

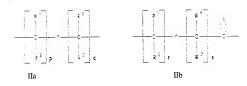
L is R¹²(R¹³)_a; wherein:

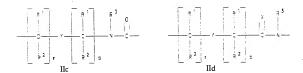
 R^{12} is hydrogen, hydroxy, (C_1 - C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group;

R¹³, if present, is a conjugate; and a is 0 or 1:

A and B are selected such that:

- (a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R³N⁺; or
- (b) A is a group of formula (IId) and B is CH;





where:

X is O, S, Se, NR3, CH2 or C(CH3)2;

Y is a single bond, O, S or NR4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

 R^1 and R^2 independently are hydrogen, (C_1-C_4) alkyl, hydroxy-substituted (C_1-C_4) alkyl, alkoxy-substituted (C_1-C_4) alkyl, alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is $(CR^6R^7)_y$:

D is (CR⁶R⁷)₂; wherein:

 R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2\text{-}C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1\text{-}C_6)$ alkoxy, $(C_1\text{-}C_6)$ alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system:

 $R^3 \ and \ R^4 \ independently \ are \ hydrogen, \ a \ conjugate. \ (C_1-C_4)alkyl, \ hydroxy- \ or \ alkylthio-substituted \ (C_1-C_4)alkyl, \ hydroxy, \ alkoxy, \ alkylthio \ or \ amino; \ and$

 $R^{5} \ is \ hydrogen, \ a \ conjugate, \ (C_{1}-C_{6}) alkyl, \ hydroxy-. \ alkoxy-. \ or \ alkylthiosubstituted \ (C_{1}-C_{6}) alkyl;$

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof:

F independently is NHR³ or NPgR³, where Pg is an amino protecting group: or F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator: or at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety; and wherein at least one group R³ is a conjugate.

58. (new) A peptide nucleic acid conjugate comprising a plurality of monomers of formula:

wherein:

L is R¹²(R¹³)_a; wherein:

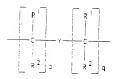
 R^{12} is hydrogen, hydroxy, $(C_1\text{-}C_4)$ alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group:

R13, if present, is a conjugate; and

a is 0 or 1.

A and B are selected such that:

- (a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R3N+; or
- (b) A is a group of formula (IId) and B is CH;



C Y C C C

ΙΙa



where:

X is O, S, Se, NR3, CH2 or C(CH3)2;

Y is a single bond, O, S or NR4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

 $R^1 \ and \ R^2 \ independently \ are \ hydrogen, (C_1-C_4) alkyl. \ hydroxy-substituted (C_1-C_4) alkyl. \ alkoxy-substituted (C_1-C_4) alkyl. \ hydroxy, alkylthio, amino, halogen or a conjugate;$

C is (CR⁶R⁷)_y;

D is (CR6R7)z; wherein:

 R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system.

 R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino: and

 $\label{eq:reconstruction} R^5 \text{ is hydrogen, a conjugate, } (C_1\text{-}C_6) \text{alkyl, hydroxy-. alkoxy-, or alkylthio- substituted} \\ (C_1\text{-}C_6) \text{alkyl;}$

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10:

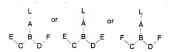
E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof;

F independently is NHR³ or NPgR³, where Pg is an amino protecting group; or F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme. a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and wherein said conjugate optionally includes a lipiding registation.

wherein said conjugate optionally includes a linking moiety; and wherein at least one of said groups A or said groups B include a conjugate.

59. (new) A peptide nucleic acid conjugate comprising a plurality of monomers of formula:



wherein:

L is R¹²(R¹³)_a; wherein:

 R^{12} is hydrogen, hydroxy, $(C_1\text{-}C_4)$ alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group:

R13, if present, is a conjugate; and

a is 0 or 1:

A and B are selected such that:

- (a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R³N⁺; or
- (b) A is a group of formula (IId) and B is CH;





IIa

IIb



IIc



IId

where

X is O. S. Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR4;

p and q independently are zero or an integer from 1 to 5:

r and s independently are zero or an integer from 1 to 5:

 $= R^1 \text{ and } R^2 \text{ independently are hydrogen, } (C_1-C_4)\text{alkyl, hydroxy-substituted } (C_1-C_4)\text{alkyl, alkoxy-substituted } (C_1-C_4)\text{alkyl, alkoxy-substituted } (C_1-C_4)\text{alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate:}$

C is (CR⁶R⁷)_y;

D is (CR⁶R⁷), wherein:

 R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid. (C₂-C₆) alkyl. aryl. aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy. (C₁-C₆) alkylthio, a conjugate, NR $^2R^4$ and SR 5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system.

 R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino; and

 R^5 is hydrogen, a conjugate, $(C_1\text{-}C_6)$ alkyl, hydroxy-, alkoxy-, or alkylthio- substituted $(C_1\text{-}C_6)$ alkyl;

PATENT

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10:

E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof:

F independently is NHR³ or NPgR³, where Pg is an amino protecting group: or

F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety; and wherein at least one of group R^1 or group R^2 is a conjugate.

60. (new) A peptide nucleic acid conjugate comprising a plurality of monomers of formula:

wherein:

L is R12(R13)a; wherein:

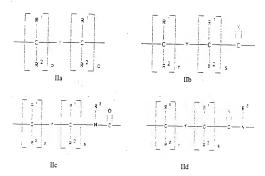
 R^{12} is hydrogen, hydroxy, $(C_1\text{-}C_4)$ alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group;

R13, if present, is a conjugate; and

a is 0 or 1:

A and B are selected such that:

- (a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R³N⁺; or
- (b) A is a group of formula (IId) and B is CH:



where:

X is O, S. Se. NR3, CH2 or C(CH3)2;

Y is a single bond, O, S or NR4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

 R^1 and R^2 independently are hydrogen, (C1-C4)alkyl. hydroxy-substituted (C1-

 C_4)alkyl, alkoxy-substituted (C_1 - C_4)alkyl, alkylthio-substituted (C_1 - C_4)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is $(CR^6R^7)_v$;

D is (CR⁶R⁷)_z; wherein:

 R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C2-C6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C1-C6) alkoxy, (C1-C6) alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

 R^3 and R^4 independently are hydrogen, a conjugate, $(C_1\text{-}C_4)alkyl,$ hydroxy- or alkoxyor alkylthio-substituted $(C_1$ - C_4) alkyl, hydroxy, alkoxy, alkylthio or amino; and

 R^5 is hydrogen, a conjugate, $(C_1 - C_6)$ alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C1-C6)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof:

F independently is NHR^3 or $NPgR^3$, where Pg is an amino protecting group; or F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, or a porphyrin; or

at least one of A and L comprises a conjugate selected from a reporter enzyme. a reporter molecule. a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid. a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety; and wherein at least one of R3, R4, R5, R6, and R7 is a conjugate.

(new) A peptide nucleic acid conjugate comprising a plurality of monomers of 61. formula:

wherein:

L is R12(R13)a; wherein:

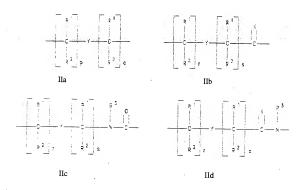
 \mathbb{R}^{12} is hydrogen, hydroxy, $(C_1\text{-}C_4)$ alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a

nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group;

a is 0 or 1;

A and B are selected such that:

- (a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R³N⁺; or
- (b) A is a group of formula (IId) and B is CH;



where:

X is O. S, Se, NR3, CH2 or C(CH3)2:

Y is a single bond, O, S or NR4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

 R^1 and R^2 independently are hydrogen, $(C_1$ - C_4)alkyl, hydroxy-substituted $(C_1$ - C_4)alkyl, alkoxy-substituted $(C_1$ - C_4)alkyl, alkoxy-substituted $(C_1$ - C_4)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is (CR6R7),;

D is (CR⁶R⁷)_z; wherein:

 R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2\text{-}C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1\text{-}C_6)$ alkoxy, $(C_1\text{-}C_6)$ alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system:

R³ and R⁴ independently are hydrogen, a conjugate, (C₁-C₄)alkyl, hydroxy- or alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio or amino; and

 $R^5 \ \text{is hydrogen. a conjugate, } (C_1\text{-}C_6) \text{alkyl, hydroxy-, alkoxy-, or alkylthiosubstituted } (C_1\text{-}C_6) \text{alkyl;}$

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO2OH or an activated or protected derivative thereof;

F independently is NHR³ or NPgR³, where Pg is an amino protecting group; or F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and wherein said conjugate optionally includes a linking moiety; and

wherein at least one of said groups C or said groups D include a conjugate.

62. (new) A peptide nucleic acid conjugate comprising a plurality of monomers of formula:

wherein:

L is R12(R13)a; wherein:

PATENT

Docket No.: ISIS-1158

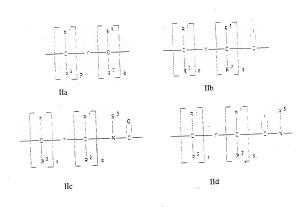
 R^{12} is hydrogen, hydroxy, (C_1-C_4) alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, or a nucleobase-binding group:

R¹³, if present, is a conjugate; and

a is 0 or 1;

A and B are selected such that:

- (a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R³N⁺; or
- (b) A is a group of formula (IId) and B is CH;



where:

X is O, S, Se, NR3, CH2 or C(CH3)2;

Y is a single bond, O, S or NR4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

PATENT

Docket No.: ISIS-1158

 $R^1 \ and \ R^2 \ independently \ are \ hydrogen, \ (C_1-C_4)alkyl. \ \ hydroxy-substituted \ (C_1-C_4)alkyl. \ alkylthio-substituted \ (C_1-C_4)alkyl. \ hydroxy. \ alkoxy, \ alkylthio, \ amino, \ halogen \ or \ a \ conjugate;$

C is (CR⁶R⁷)_v;

D is (CR6R7)z; wherein:

 R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2\text{-}C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1\text{-}C_6)$ alkoy, $(C_1\text{-}C_6)$ alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system.

 R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4) alkyl, hydroxy, alkoxy, alkylthio or amino: and R^5 is hydrogen, a conjugate, (C_1-C_6) alkyl, hydroxy-, alkoxy-, or alkylthiosubstituted (C_1-C_6) alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO₂OH or an activated or protected derivative thereof;

F independently is NHR³ or NPgR³, where Pg is an amino protecting group; or

F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, or a porphyrin; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety.